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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,265	11/12/2003	Sam Hwang	224738	5821

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EXAMINER

HARLE, JENNIFER I

ART UNIT

PAPER NUMBER

1654

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/706,265

Applicant(s)

HWANG, SAM

Examiner

Jennifer I. Harle

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11 and 36-39 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 36-39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Claims 1-11 and 36-39 are pending. Claims 12-35 are cancelled pursuant to Applicant's Amendment filed September 12, 2005.

#### ***Election/Restrictions***

2. This application contains claims 12-35 drawn to an invention nonelected with traverse in Paper No. January 26, 2005. The claims have been cancelled in Applicant's amendment, thus appropriate action for the nonelected claims has been taken pursuant to (37 CFR 1.144). See MPEP § 821.01.

#### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 103***

3. Applicant's arguments filed September 12, 2005 have been fully considered but they are not persuasive. The examiner Official Action, mailed May 17, 2005, is incorporated in its entirety by reference.

Applicant argues that contrary to the examiner's discussion of the Koshiba that Koshiba discloses only *in vitro* testing of T22 and expressly states that the *in vivo* role of the T22 poly peptide with respect to metastasis (i.e. tumor spread is unknown: quoting "The mode of action of chemokines depends heavily on the local environment ... In this situation, *in vitro* migration assays may not predict *in vivo* function." Applicant then proceeds to argue tat Koshiba states that *in vivo* testing is required to determine whether or not T22 suppresses tumor spreads and to clarify its role in pancreatic cancer (pg. 3535, col. 1, lines 23-27). Thus, Applicant concludes that Koshiba would not have provided, at the time of the invention, a reasonable expectation that

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T22 could be used to inhibit metastasis, as required to establish a *prima facie* case of obviousness but rather an invitation to try.

The examiner respectfully disagrees. Applicant had mischaracterized the disclosure of Koshiha and that the examiner has set forth a clear rationale as to why it inhibits metastasis of a tumor cell under §103(a). Koshiha discloses that it is well known that the interaction between cancer cells and stromal cells is deeply involved in tumor invasion and metastasis and that they were able to demonstrate that MRC9 fibroblast cells significantly increased the migratory capability of CFPAC-1 cells and that T22 significantly reduced this capability when they are cocultured. Pg. 3535, col. 1, lines 2-8. Additionally Koshiha discloses that the *in vitro* findings indicate that SDF-1 acts as a chemo attractive factor for pancreatic cancer cells and endothelial cells and is, at least in part, involved in the mechanism of cancer cell migration resulting from fibroblast coculture. Id. at lines 8-12. While Koshiha does state that “The mode of action of chemokines depends heavily on the local environment.”, he continues to disclose that the secreted SDF-1 is thought to act by creating a gradient for CXCR4-bearing cells and the secreted protein may be localized by binding to extracellular matrix, before disclosing that “In this situation, *in vitro* migration assays may not predict *in vivo* function.” Id at lines 12-16. **It is important to note** that he follows these statements with “**In vitro findings, however, indicate** SDF-1 acts as a chemoattractive factor for pancreatic cancer cells and endothelial cells and is, at least in part, involved in the mechanism of cancer cell migration resulting from fibroblast coculture. In conclusion our results suggest that the SDF-1/CXCR4 receptor ligand system may have a possible role in pancreatic cancer progression through tumor cell migration and angiogenesis. **Because T22** suppressed the migration of both pancreatic cancer cells and

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endothelial cells *in vitro*, **additional *in vivo* studies are warranted** to examine whether T22 suppresses the tumor spread and tumor angiogenesis **to clarify** the role of the SDF-1/CXCR4 receptor ligand system in pancreatic cancer.” Id at lines 17-25. There is then an express statement that one should perform additional *in vivo* tests based upon their conclusions about the mechanisms of SDF-1/CXCR4 and T22. Id. at 21-25 and Previous Office Action rationale for Koshiba. This is not a statement that it is obvious to try but that one should go out and perform these tests on *in vivo* models.

Applicants further argue that there is no other evidence provided as to the type of testing that would be required or the parameters that should be varied in order to arrive at a method of using T22 to inhibit metastasis, only that which is found in Applicant’s disclosure. Applicants assert that neither Murphy or Clark-Lewis provide this missing teaching.

Applicant’s only require that inhibiting metastasis of tumor cells in a mammal and inhibiting growth of a tumor cell either in a cell line or in a mammal and T22 is administered, the recite a mechanism of action, i.e. that the tumor cell expresses CXCR4 and/or the growth is stimulated by SDF-1. As set forth above, Koshiba provides the requisite for *in vivo* administration. For a complete analysis see the previous Office Action incorporated by reference in its entirety, as set forth above. Applicant’s arguments that neither Murphy nor Clark-Lewis provide any missing teaching without more is not persuasive. Both Murphy and Clark-Lewis disclose use of CXCR-4 antagonists, of which T-22 is one, in animal models to inhibit metastasis of tumor cells and inhibit the growth of tumor cells. Moreover, since both Murphy and Clark-Lewis disclose CXCR-4 antagonists that have *in-vivo* efficacy then there is a reasonable expectation of success that T22, which has the same mode action *in vitro*, would react similarly

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*in vivo*. The teachings of these references was not disputed nor was the motivation to combine.

Only the teaching of Koshiha was at issue. Thus, the rejections of claims 1-11 and 36-39 is maintained and made final.

### ***Conclusion***

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer I. Harle whose telephone number is (571) 272-2763. The examiner can normally be reached on Monday through Thursday, 6:30 am to 5:00 pm,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jennifer I. Harle  
Examiner  
Art Unit 1654

November 4, 2005

A handwritten signature in black ink, appearing to read "Bruce Campbell". The signature is fluid and cursive, with the first name "Bruce" and last name "Campbell" clearly distinguishable.

**SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600**